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| 09/801,852 | 03/08/2001 | Shu-Jen David Chiang | ON0163NP | 6300 |

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| EXAMINER |
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SLOBODYANSKY, ELIZABETH

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| ART UNIT | PAPER NUMBER |
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1652

DATE MAILED: 05/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n No.

09/801,852

Applicant(s)

CHIANG

Examin r

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 19 February 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

- 4) ☒ Claim(s) 1,3-6 and 8-13 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3-6,8-13 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

The amendment filed February 19, 2003 amending claims 1 and 8-13 and canceling claims 2 and 7 has been entered.

Claims 1, 3-6 and 8-13 are pending.

Claim Objections

Claim 11 is objected to because of the following informalities: "SEQ ID No:" is typed instead of "SEQ ID NO:".

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12 and 13 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is reiterated from the Office action mailed September 10, 2002.

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Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 1, 3-6 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Politino et al. (A).

Politino et al. (A), (WO 98/12345, form PTO-1449 filed January 14, 2002, reference AM) teach a method for producing of desacetylcephalosporin C using a cephalosporin esterase from *Rhodospiridium toruloides* (Example 2). *Cephalosporin acremonium* is a former name of *Acremonium chrysogenum* (specification, page 1, line 16). They teach that cephalosporin C is completely hydrolyzed by the esterase within 30 min at 30° C, pH 6.5, with no side products observed by HPLC (page 16, lines 14, 25-26). They teach the method for producing the esterase by culturing cells of *Cephalosporin acremonium* transformed with a DNA encoding a cephalosporin

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esterase from *Rhodospiridium toruloides* (claims 26-28). Therefore, they teach a method for producing of desacetylcephalosporin C by culturing cells of *Cephalosporin acremonium* (*Acremonium chrysogenum*) transformed with a DNA encoding a *Rhodospiridium* esterase (for example, Example 2, claims 26-28). *Acremonium chrysogenum* is producing cephalosporin C and contains nucleic acid encoding enzymes for cephalosporin C biosynthesis and a recombinant nucleic acid encoding *Rhodospiridium* esterase. A DNA encoding cephalosporin esterase from *Rhodospiridium toruloides* is 100% identical to SEQ ID NO:3 and differs by one nucleotide from SEQ ID NO:1.

The conditions of "30° C" that is "about 29° C" and "pH 6.5" that is in the range of "about 5.5 to about 7.5" meet the limitations for the experimental parameters recited in claim 1. The teachings of Politino et al. further meet the limitations of the chemical breakdown of cephalosporin C of less than 40%, 30%, 20%, 10% or 5% as required by claims 1 and 3-6 because no side products were observed by HPLC.

Claims 1, 3-6 and 9-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Politino et al.(B)

Politino et al. (B), (US Patent 5,869,309, form PTO-1449 filed June 14, 2001, reference AG) is US counterpart of WO 98/12345, *supra*. They teach a method for producing of desacetylcephalosporin C using a cephalosporin esterase from

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Rhodospiridium toruloides (Example 2). They teach that cephalosporin C is completely hydrolyzed by the esterase within 30 min at 30° C, pH 6.5, with no side products observed by HPLC (column 9, line 60, through column 10, line 14). They teach the method for producing the esterase by culturing cells of *Cephalosporin acremonium* transformed with a DNA encoding a cephalosporin esterase from *Rhodospiridium toruloides* (claims 17-24). Therefore, they teach a method for producing of desacetylcephalosporin C by culturing cells of *Cephalosporin acremonium* (*Acremonium chrysogenum*) transformed with a DNA encoding a *Rhodospiridium toruloides* esterase (for example, Example 2, claims 17-24). *Acremonium chrysogenum* is producing cephalosporin C and contains nucleic acid encoding enzymes for cephalosporin C biosynthesis and a recombinant nucleic acid encoding *Rhodospiridium* esterase. A DNA encoding cephalosporin esterase from *Rhodospiridium toruloides* (SEQ ID NOs: 1 or 3) is 100% identical to SEQ ID NOs: 1 or 3, respectively, of the instant invention.

The conditions of "30° C" that is "about 29° C" and "pH 6.5" that is in the range of "about 5.5 to about 7.5" meet the limitations for the experimental parameters recited in claim 1. The teachings of Politino et al. further meet the limitations of the chemical breakdown of cephalosporin C of less than 40%, 30%, 20%, 10% or 5% as required by claims 1 and 3-6 because no side products were observed by HPLC.

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Politino et al. (A) or (B) in view of Smith et al.

The teachings of Politino et al. (A) and (B) are outlined above.

Smith et al. (US Patent 4,533,632, form PTO-1449 filed June 14, 2001, reference AC) teach a process for the preparation of desacetylcephalosporin C by fermenting *Acremonium chrysogenum* in the presence of esterase from *Rhodospiridium toruloides* (claims 1-7). The process of fermentation is carried out at 15°-45° C and pH 4-9.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use *Acremonium chrysogenum* transformed with a DNA encoding *Rhodospiridium toruloides* esterase in the production of desacetylcephalosporin C. This would allow to increase and standardize the production of the esterase used in the method taught by Smith et al. Such host cells are taught by Politino et al. (A, B). It would have been further obvious to find and use optimal

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conditions for producing of desacetylcephalosporin C and fermenting *Acremonium chrysogenum* within the range of standard conditions taught by Smith et al.

Response to Arguments

Applicant's arguments filed February 19, 2003 have been fully considered but they are not persuasive.

With regard to the deposit requirements Applicants argue that as described in the specification on page 10, lines 14-19, pBMesterase11 has been deposited with ATCC (Remarks, page 3). This is not persuasive because while this plasmid has been deposited it is not necessarily publicly available. Applicants further refer to US Patent 5,516,679 and Staben et al. to assert that the plasmids are publicly available. This is not persuasive because just the description of plasmids in US patent or a publication does not render them publicly available. Furthermore, as an essential material, the plasmids must be described in the instant application.

With regard to the 102 (b, e) rejections, Applicants argue referring to the experimental conditions, that neither Politino et al. (A) nor Politino et al. (B) "disclose all elements of the claims" (pages 6-8). The rejections have been reworded to address the condition issues. In view of the rejections, *supra*, Applicants arguments are not persuasive.

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With regard to the 103(a) rejection, upon Applicant's request the examiner clarifies that the rejection refers to either Politino et al. (A) or Politino et al. (B). As mentioned above, both references disclose the same invention.

Further, Applicants argue that "Neither Politino (WO 98/12345 or 5,869,309) nor Smith, alone or in combination, disclose Applicants' claimed invention" (page 8). The examiner disagrees with said arguments for the reasons explained in the rejection. Furthermore, as the references used in the 103(a) rejection, neither Politino et al. nor Smith et al. have to disclose the same invention but only to make it obvious. It would have been obvious to optimize known standard conditions as applied to the specific experiment. The conditions recited in claim 8 are obvious over the conditions disclosed in Politino et al. (A), (B) and are within the range disclosed by Smith et al. Furthermore, the use of the specific conditions recited in claim 8 does not lead to unexpected results.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

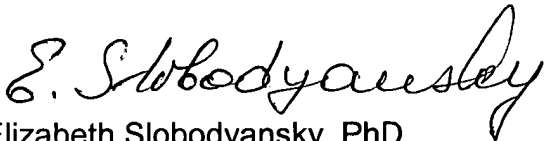
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shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in cursive script that reads "E. Slobodyansky".

Elizabeth Slobodyansky, PhD
Primary Examiner

May 14, 2003